

AMENDMENTS TO THE CLAIMS

Please replace all prior versions, and listings, of claims in the application with the following list of claims:

1. (Currently amended) An isolated anti-Tumor Necrosis Factor-alpha (anti-TNF-alpha) polypeptide comprising at least two ~~[[one]]~~ anti-TNF-alpha single domain antibodies ~~antibody~~ which are ~~[[is a]]~~ *Camelidae* variable domains derived from a heavy chain antibody devoid of a light chain (VHH) or ~~[[a]]~~ humanized *Camelidae* VHHs, wherein the polypeptide does not include a light chain.
2. (Previously presented) An anti-TNF-alpha polypeptide according to claim 1 wherein at least one single domain antibody comprises the amino acid sequence of any of SEQ ID NOs: 1 to 16 and 79 to 84.
3. (Previously presented) An anti-TNF-alpha polypeptide according to claim 1 further comprising at least one single domain antibody directed against a serum protein.
4. (Previously presented) An anti-TNF-alpha polypeptide according to claim 3 wherein said serum protein is any of serum albumin, serum immunoglobulins, thyroxine-binding protein, transferrin, or fibrinogen.
5. (Previously presented) An anti-TNF-alpha polypeptide according to claim 3 wherein the anti-serum protein single domain antibody comprises the amino acid sequence of any of SEQ ID NOs: 26 to 29 and 85 to 97.
6. (Canceled)
7. (Previously presented) An anti-TNF-alpha polypeptide according to claim 1 further comprising at least one single domain antibody selected from the group consisting of anti-

interferon-gamma (anti-IFN-gamma) single domain antibody, anti-TNF-alpha receptor single domain antibody and anti-IFN-gamma receptor single domain antibody.

8. (Canceled)

9. (Withdrawn and Currently amended) An anti-TNF-alpha polypeptide according to claim 1 [[8]] comprising the amino acid sequence of any of SEQ ID NOs: 73 to 76.

10. (Previously presented) An anti-TNF-alpha polypeptide according claim 1 wherein at least one single domain antibody is a humanized *Camelidae* VHH.

11. (Canceled)

12. (Previously presented) A composition comprising an anti-TNF-alpha polypeptide according to claim 1 and at least one single domain antibody from the group consisting of anti-interferon-gamma (anti-IFN-gamma) single domain antibody, anti-TNF-alpha receptor single domain antibody and anti-IFN-gamma receptor single domain antibody.

13. (Withdrawn and Previously presented) An anti-TNF-alpha polypeptide according to claim 7 wherein the at least one anti-IFN-gamma single domain antibody comprises the amino acid sequence of any of SEQ ID NOs: 44 to 72.

14. (Canceled)

15. (Canceled)

16. (Currently amended) An anti-TNF-alpha polypeptide according to claim 1 wherein the at least [[one]] two anti-TNF-alpha single domain antibodies are ~~antibody is a~~ *Camelidae* VHHs.

17.-25. (Canceled)

26. (Withdrawn) A method for treating and/or preventing and/or alleviating disorders relating to inflammatory reactions comprising administering to a subject in need of such treatment an effective amount of the an anti-TNF-alpha polypeptide of claim 1.

27. (Canceled)

28. (Withdrawn) A method for treating and/or preventing and/or alleviating the symptoms of disorders susceptible to modulation by a TNF-alpha modulating substance. comprising administering to a subject in need of such treatment an anti-TNF-alpha polypeptide of claim 1 that passes through the gastric environment without the substance being inactivated.

29. (Canceled)

30. (Withdrawn) A method for treating and/or preventing and/or alleviating disorders susceptible to modulation by a TNF-alpha modulating substance delivered to the vaginal and/or rectal tract, or the nose, upper respiratory tract and/or lung, comprising administering to the vaginal and/or rectal tract, or the nose, upper respiratory tract and/or lung, of a subject in need of such treatment an effective amount of an anti-TNF-alpha polypeptide of claim 1.

31.-33. (Canceled)

34. (Withdrawn) A method for treating and/or preventing and/or alleviating the symptoms of disorders susceptible to modulation by a TNF-alpha modulating substance delivered to the intestinal mucosa, wherein said disorder increases the permeability of the intestinal mucosa, comprising administering to the intestinal mucosa of a subject in need of such treatment an anti-TNF-alpha polypeptide of claim 1.

35. (Canceled)

36. (Withdrawn) A method for treating and/or preventing and/or alleviating the symptoms of disorders susceptible to modulation by a TNF-alpha modulating substance, comprising administering to a subject in need of such treatment an anti-TNF-alpha polypeptide of claim 1 that passes through the tissues beneath the tongue effectively.

37. (Canceled)

38. (Withdrawn) A method for treating and/or preventing and/or alleviating the symptoms of disorders susceptible to modulation by a TNF-alpha modulating substance, comprising administering to a subject in need of such treatment an anti-TNF-alpha polypeptide of claim 1 that passes through the skin effectively.

39. (Withdrawn) A method according to any of claims 26, 28, 30, 34, 36, and 38, wherein said disorders are any of inflammation, rheumatoid arthritis, Crohn's disease, ulcerative colitis, inflammatory bowel syndrome, multiple sclerosis, Addison's disease, Autoimmune hepatitis, Autoimmune parotitis, Diabetes Type I, Epididymitis, Glomerulonephritis, Graves' disease, Guillain-Barre syndrome, Hashimoto's disease, Hemolytic anemia, Systemic lupus erythematosus, Male infertility, Multiple sclerosis, Myasthenia Gravis, Pemphigus, Psoriasis, Rheumatic fever, Rheumatoid arthritis, Sarcoidosis, Scleroderma, Sjogren's syndrome, Spondyloarthropathies, Thyroiditis, and Vasculitis.

40. (Previously presented) A composition comprising the anti-TNF-alpha polypeptide of claim 1 and a suitable pharmaceutical vehicle.

41. (Withdrawn) A method of diagnosing a disorder characterised by the dysfunction of Tumor Necrosis Factor-alpha comprising:

(a) contacting a sample with an anti-TNF-alpha polypeptide of claim 1,

- (b) detecting binding of said polypeptide to said sample, and
- (c) comparing the binding detected in step (b) with a standard, wherein a difference in binding relative to said sample is diagnostic of a disorder characterised by dysfunction of Tumor Necrosis Factor-alpha.

42.-43. (Canceled)

44. (Withdrawn) A method for purification of Tumor Necrosis Factor-alpha, comprising contacting a sample with the anti-TNF-alpha polypeptide of claim 1.

45. (Withdrawn) A method for inhibiting the interaction between Tumor Necrosis Factor-alpha and one or more Tumor Necrosis Factor-alpha receptors, comprising contacting Tumor Necrosis Factor-alpha with the anti-TNF-alpha polypeptide of claim 1.

46.-49. (Canceled)